MERCK / Schering-Plough Pharmaceuticals

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AC-09-40

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Roger Citron, R.Ph.
Montana Department of Public Health
and Human Services
1400 Broadway
P.O. Box 202951
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Dear Mr. Citron:

Our Senior NAE Representative, Elaine Zompolas, has referred your request for information regarding VYTORIN (ezetimibe/simvastatin). Your inquiry concerned dosage and administration of VYTORIN.

The patient should be placed on a standard cholesterol-lowering diet before receiving VYTORIN and should continue on this diet during treatment with VYTORIN. The dosage should be individualized according to the baseline LDL-C level, the recommended goal of therapy, and the patient's response. VYTORIN should be taken as a single daily dose in the evening, with or without food.

The dosage range is 10/10 mg/day through 10/80 mg/day. The recommended usual starting dose is 10/20 mg/day. Initiation of therapy with 10/10 mg/day may be considered for patients requiring less aggressive LDL-C reductions. Patients who require a larger reduction in LDL-C (greater than 55%) may be started at 10/40 mg/day. After initiation or titration of VYTORIN, lipid levels may be analyzed after 2 or more weeks and dosage adjusted, if needed.

See below for dosage recommendations for patients receiving certain concomitant therapies and conditions.

The recommended dosage for patients with homozygous familial hypercholesterolemia is VYTORIN 10/40 mg/day or 10/80 mg/day in the evening. VYTORIN should be used as an adjunct to other lipid-lowering treatments (e.g., LDL apheresis) in these patients or if such treatments are unavailable.

No dosage adjustment is necessary in patients with mild hepatic insufficiency.

No dosage adjustment is necessary in patients with mild or moderate renal insufficiency. However, for patients with severe renal insufficiency, VYTORIN should not be started unless the patient has already tolerated treatment with simvastatin at a dose of 5 mg or higher. Caution should be exercised when VYTORIN is administered to these patients and they should be closely monitored.

No dosage adjustment is necessary in geriatric patients.

Dosing of VYTORIN should occur either ≥2 hours before or ≥4 hours after administration of a bile acid sequestrant.

Caution should be exercised when initiating VYTORIN in the setting of cyclosporine. In patients taking cyclosporine or danazol, VYTORIN should not be started unless the patient has already tolerated treatment with simvastatin at a dose of 5 mg or higher. The dose of VYTORIN should not exceed 10/10 mg/day.

In patients taking amiodarone or verapamil concomitantly with VYTORIN, the dose should not exceed 10/20 mg/day.

The safety and effectiveness of ezetimibe administered with fibrates have not been established. Therefore, the combination of VYTORIN and fibrates should be avoided.

There is an increased risk of myopathy when simvastatin is used concomitantly with fibrates (especially gemfibrozil). Therefore, although not recommended, if VYTORIN is used in combination with gemfibrozil, the dose should not exceed 10/10 mg daily.

The above information is supplied to you as a professional service in response to your specific request. Merck/Schering-Plough Pharmaceuticals does not recommend the use of its products in any manner other than as described in the prescribing information. Enclosed for your convenience is prescribing information for VYTORIN.

Sincerely,

Ruth Stolz, MD

Ruth Stolz, M.D.
Director
Medical Services

Enclosure: Circulars